

Worried about Warfarin?

Know the benefits of genetic testing.

Iverson Warfarin Dosing Panel



Warfarin Dosing Can Be a Challenge

If you have patients who take warfarin (brand name Coumadin®), you know that achieving a stable INR (international normalized ratio) can be a challenge. Too little warfarin leaves patients at risk for thrombosis. Too much can promote adverse bleeding events. On average, 50% of bleeding events associated with warfarin use occur within the first 90 days of treatment.

Achieving a stable INR often requires trial and error with frequent and costly testing. The risk of bleeding complications is high enough that many patients who could benefit from warfarin do not receive it at all.

Today, with genetic testing, you have another tool to make warfarin dosing safer, overall less costly and provide more effective anti-thrombotic therapy for your patients.

Why Should You Test?

Optimal Dosage

Gives you critical pharmacogenetic information to help compute the optimal warfarin dose.

Safety

Provides additional security for your patient and for you, diminishing emergency room visits and potential litigation.

It's Covered

Medicare, Medicaid (check state by state) and many insurers cover the Iverson test.

Early Hospital Discharge

May help bring patients to therapeutic INR more rapidly, allowing them to go home sooner and enabling hospitals to serve new patients.

Cost Savings

May reduce overhead costs by managing the patient population's therapeutic range more effectively, and reduce levels of emergency medical intervention.

Drug Metabolism: CYP2C9

Patients with variations in CYP2C9 account for approximately 15% of variability in warfarin dose response. These variations differ with racial background. Approximately 20% of Caucasians, 5% of African-Americans and 2% of Asians carry at least one variant copy of CYP2C9. Patients with CYP2C9 gene variations may:

- require more time to achieve a stable INR.
- be at increased risk of bleeding.
- need lower doses of warfarin to achieve and maintain therapeutic INR.

Drug Response: VKORC1

Patients with variations in VKORC1 account for up to 25% of variability in warfarin dose response. These variations also differ with racial background. Approximately 37% of Caucasians, 14% of African-Americans and 89% of Asians carry at least one variant copy of VKORC1. Patients with VKORC1 gene variations may:

- have an increased risk for anticoagulant overdose.
- require lower doses of warfarin to achieve and maintain therapeutic INR.



A Closer Look at How Genotypes Affect Warfarin Metabolism

Warfarin is highly effective at antagonizing the vitamin K-dependent clotting pathway. A natural substance, it is given as a mixture of R and S stereoisomers (the chemical equivalent of mirror images).

S-warfarin is three to five times more potent than its cousin, R-warfarin, in inhibiting the drug's target of action: the vitamin K epoxide reductase complex 1. Phase I metabolism of S-warfarin is predominantly via the CYP2C9 enzyme. Genetic variations in this enzyme can affect the rate at which warfarin is inactivated and can play a major role in determining what an individual's maintenance dose of warfarin will be.

Patients with some genetic variants are more likely to need lower doses of warfarin, take a longer time to reach target INR on starting therapy and may have an increased risk of bleeding complications.

The vitamin K epoxide reductase complex 1 is responsible for converting vitamin K from an oxidized to a reduced state. Reduced vitamin K is key to the formation of many of the proteins in the clotting cascade, and without it, overall coagulation is significantly inhibited. Warfarin inhibits the action of the major subunit of the vitamin K epoxide reductase complex 1: VKORC1. Variations in the VKORC1 subunit have been shown to be differentially sensitive to the action of warfarin.

Together, VKORC1 and CYP2C9 account for up to 40% of the individual variability in warfarin response. Other important variables include age, gender, height and weight, drug interactions and diet.¹

21% of patients who receive anticoagulation therapy experience major or minor bleeding events.⁴

Iverson Warfarin Dosing Panel

Helps You Make Better Dosing Decisions for Your Patients

Our easy-to-use test will quickly allow you to know if the patient you are treating has genetic variations that play key roles in determining the correct maintenance dose. It may offer important information regarding initial dosing estimates and increase the safety and efficacy of the warfarin therapy. It also may provide some additional measure of reassurance in dosing if the test reveals that the patient does not have the relevant variations. The test can help you:

- prescribe a standardized dosing regimen with greater confidence.
- help your patients identify their personal maintenance dosage more quickly.
- reduce the clinical risk associated with inducing a life-threatening bleeding event.

The Benefits of Testing: Optimal Dose, Fewer Adjustments, Faster Time to INR

The Iverson Warfarin Dosing Panel can help you predict the optimal warfarin dose, may shorten the time to achieve stable dosing, can reduce the need for dose adjustments, can increase the time each patient spends in the target INR range, and has the potential to improve the overall safety and efficacy of warfarin therapy.

Right Dosage? Look to Your Patient's Genes

There is a 10-fold inter-patient variability in the dosing required to attain a therapeutic response.² Research has clearly shown that up to 40% of the individual variability in warfarin response can be accounted for by variations in two enzymes: CYP2C9 and VKORC1. CYP2C9 affects how warfarin is metabolized. VKORC1 affects how some patients respond to the drug.

The Iverson Warfarin Dosing Panel tests specifically for the following commonly identified genetic variants:

- CYP2C9 *2 & *3
- VKORC1 3673

The AEI-Brookings Joint Center for Regulatory Studies recently estimated that the use of CYP2C9 genotyping has the potential to avoid 85,000 serious bleeding events and 17,000 strokes annually and to significantly reduce health care spending.³

References

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We encourage you and your staff to contact us at any time.
We are always just a phone call or an email away.



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In August 2007, the U.S. Food and Drug Administration (FDA) revised the warfarin label to recommend genetic testing prior to initiation of warfarin therapy.⁵